

independent claim 152 which is directed to a dispenser having a plurality of dispensing units and dependent claims 153-206 which mirror dependent claims already pending in the application. Applicants would like to address Cozzette *et al.* U.S. Patent No. 5,200,051 and Sanz U.S. Patent No. 3,615,240 each of which were cited in co-pending application 09/498,554 in view of the amended claims.

Cozzette *et al.* does not teach a dispenser adjusted to dispense droplets no greater than 5 nl. Furthermore, Cozzette does not suggest that it may be modified to dispense droplets no greater than 5 nl. Cozzette *et al.* states that drops between about 5 to 500 nl can be dispensed. However, Cozzette *et al.* dispenses volumes sufficient to cover electrodes. Cozzette *et al.*'s working examples indicate that at least 10 nl is used in order to effectively cover the indicator electrode of the microfabricated sensor. Cozzette *et al.* provide no teaching that amounts on the order of 5nl would be sufficient to achieve this application. The Examiner's attention is respectfully directed to col. 72 lines 16-19, col. 72 line 67 to col. 73 line 2 and col. 73 lines 52-55, where Cozzette *et al.* teaches depositing "sufficient material" (10 – 100 nl) equaling three times the diameter of the electrode. ("Sufficient material (10-100 nl) is deposited in this technique to allow for the coverage of an area about three times the diameter of the catalytic iridium electrode.") Similarly, at col. 74 lines 13-16 and 47-49, Cozzette *et al.* teaches that "sufficient material" (10 – 100 nl), equals two times the diameter of the electrode. ("Sufficient material (10-100nl) is deposited by this technique to allow for the coverage of an area about twice the diameter of the catalytic iridium electrode.") Finally, in column 75, lines 37-41, Cozzette *et al.* teaches dispensing 10 – 100 nl to overlap an electrode on all sides by at least 30  $\mu\text{m}$ . Clearly, the teachings of Cozzette are directed to completely covering the indicator

electrodes present on their sensors. Cozzette et al. provides no teaching that amounts less than 10 nl would provide this important aspect of Cozzette et al.'s invention. In fact, one would not be led to use volumes less than 10 nl because to do so would risk not completely covering the electrode.

Sanz, while disclosing a micropipette capable of dispensing volumes on the order of one nl, would not lead one of skill in the art to modify Cozzette et al. to include a dispenser adjusted to dispense less than 10 nl in the practice of Cozzette et al.'s invention. Again, Cozzette et al. teaches in its working examples that amounts of 10 nl at a minimum be dispensed to completely cover the electrodes. One would not be motivated to dispense 1 nl volumes as disclosed by Sanz (i.e., 10% of the minimum working example volume employed), since to do so would likely lead to partial electrode covering which is adverse to Cozzette et al.'s invention. Cozzette et al. does not teach using minimal reagents. Cozzette et al. teaches the dispensing of volumes sufficient to completely cover the electrodes. In fact, Cozzette et al. teaches that the volume of reagent in one embodiment be such that it covers up to three times the diameter of the electrode. Cozzette et al., therefore, does not motivate one to dispense smaller and smaller volumes of fluid so as to use minimal reagents, since Cozzette et al. advises that more reagent be dispensed than can be detected by the sensor. Cozzette et al. encourages overuse of reagent dispensed at the sensors, and does not encourage minimal reagent use.

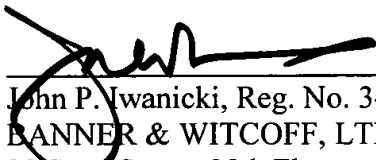
Furthermore, one of skill in the art would not look to the pipette of Sanz to modify the apparatus of Cozzette et al. Cozzette et al. teaches an automated microfabricating process which comprises a syringe which distributes liquid under the control of pulses of a pressurized gas regulated by a solenoid valve (column 58, lines 44-54, column 59, lines 18-26). In contrast,

Sanz describes a manual pipette which has a tubular handle, (1), and distributes liquid by the rotational movement of a ring, (4) (column 2, lines 3-14, Figure 15). There is nothing in Sanz that would suggest the use of its pipette in an automated system. One would not have a reasonable expectation of success using the manual pipette of Sanz in the automated system of Cozzette et al.

In addition regarding claim 152 in particular, Cozzette et al. does not teach a dispenser comprising an array of dispensing units. Thus, Applicants' invention allows the dispensing of multiple compounds simultaneously. Cozzette et al. teaches a microdispensing system which comprises multiple syringe holders (column 17, lines 28-33). Figure 13 of Cozzette et al. illustrates four separate syringe holders. Cozzette et al. does not teach a single dispensing unit containing an array of dispensing units, but instead teaches multiple (i.e., four) separate dispensing units. Furthermore, since the syringe itself is bulky relative to the wafer (see Figure 12, and compare the syringe (5) to the wafer (2)) and the syringe is placed into a single opening (13) of an even bulkier syringe holder (Figure 13), the apparatus taught by Cozzette et al. would not be amenable to depositing more than one sample at a time, and certainly would not be amenable to depositing an array of samples at the same time.

Respectfully submitted,

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